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10/502,285	07/22/2004	Ian Richard Catchpole	PG4745	9183

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EXAMINER	
ELLIS, SUEZU Y	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/502,285	CATCHPOLE, IAN RICHARD	
	Examiner	Art Unit	
	Suezu Ellis	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

The specification describes the piercing protrusion being in the form of a microblade, microcannula or microneedle, however does not appear to have support for a microneedle having a support member that is a microcannula or a microblade (claim 18).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the piercing protrusion being in the form of a microblade, microcannula or microneedle, does not reasonably provide enablement for

a microneedle having a support member that is a microcannula or microblade. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 15 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8 and 15 recite the limitation "the solid biodegradable reservoir medium". There is insufficient antecedent basis for this limitation in the claim. Examiner notes that claim 1 fails to recite the limitation of the solid reservoir medium being biodegradable, therefore claims 8 and 15 are unclear.

With respect to claim 18, it is unclear how a microneedle has a support member that is a microcannula or microblade. Please clarify.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 16, 17 19 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Dev et al. (US 6,697,669).

With respect to claims 1-3, 19 and 20, Dev et al. discloses in Figs. 6 and 12, a DNA pharmaceutical agent delivery device (electroporation device) having at least one skin-piercing microneedle which comprises a support member (electrode) coated with a solid reservoir medium (612, 622) containing a DNA pharmaceutical agent (col. 5, lines 63-65; col. 15, lines 42-46; col. 3, lines 7-10). Dev et al. discloses in Example 1, the DNA is in Tris-EDTA. Since Dev et al. demonstrates the same composition as the applicant, the Tris-EDTA is considered to be functionally equivalent to a stabilizing that inhibits the degradative effects of free radicals, as evidenced by Volkin et al. (WO 97/40839) (pg. 10, lines 14-15, claim 21).

With respect to claims 16 and 17, Dev et al. discloses the microneedle delivers the agent into the dermis or epidermis (col. 3, lines 7-10; col. 20, lines 46-47, 52-55).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-18 and 21-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Volkin et al. (WO 97/40839) in view of Dalton et al. (US 2004/0049150).

With respect to claims 1, 6-11, 15-18, 21-25, Volkin et al. discloses a DNA vaccine formulation comprising various stabilizing agents that inhibits the degradative effects of free radicals. Volkin et al. further discloses the DNA vaccine is administered to recipients via subcutaneous injection or intradermal injection, however fails to expressly disclose the details regarding the device used to perform the injection. Dalton et al. discloses a DNA pharmaceutical agent delivery device, and the process of making the delivery device, having at least one skin-piercing microneedle which comprises a support member (needle) coated with a solid reservoir medium containing the DNA pharmaceutical agent (DNA vaccine) [0025], [0061], [0041]. Dalton et al. discloses the solid reservoir medium can be an amorphous polyol, wherein the polyol is a stabilizing polyol [0027], [0030]. Dalton et al. discloses the solid reservoir medium can be a sugar selected from the group of lactose, glucose, sucrose, raffinose and trehalose [0031] and the solid reservoir medium can be in the form of a sugar glass [0033]. Dalton et al. further discloses the skin piercing microneedle is dimensioned to deliver the agent into the dermis or the epidermis [0017]. Dalton et al. also discloses the solid reservoir medium further comprises a vaccine adjuvant (CpG dinucleotide) [0075]. Dalton et al. further discloses the solid reservoir medium releases the pharmaceutical agent within a few minutes after insertion of the skin-piercing microneedle into the skin [0033]. It would have been obvious to one of ordinary skill in the art to utilize the device of Dalton

for the DNA vaccine of Volkin in order to provide a suitable means for administering the DNA vaccine to patients via injection.

With respect to claims 2-4, the modified Volkin et al. discloses the stabilizing agent is one or both of a metal ion chelator (EDTA, TRIS, succinic and malic acid) (pg. 10, lines 14-15; pg. 26, line 32 – pg. 27, line 15) and free radical scavengers (ethanol, methionine) (page 11, lines 4-9; claim 25).

With respect to claim 5, the modified Volkin et al. further discloses DNA formulations wherein the stabilizing agent that inhibit the degradative effects of free radicals is phosphate buffered ethanol solution in combination with methionine or EDTA (pg. 72, lines 14-24) and Tris buffered EDTA in combination with methionine or ethanol or a combination of methionine and ethanol (pg. 25, lines 12-19).

With respect to claim 12, the modified Volkin et al. discloses the DNA pharmaceutical agent is supercoiled plasmid DNA (pg. 34, lines 8-9).

With respect to claims 13 and 14, the modified Volkin et al. discloses that after storage at 37°C for 4 weeks, greater than 50% of the DNA remains in its supercoiled form; wherein the DNA is stabilized such that when released the ratio of monomer:dimer supercoiled form is within the range of 0.8-1.2 as evidenced by the method of detection used to detect supercoiled plasmid DNA and the stability data disclosed by the referenced invention (Tables 5, 9, 10, 13; Figs. 14, 20-24, 28; Examples 5, 11-16, 18).

With respect to claim 26, the modified Volkin et al. fails to expressly disclose the concentration of the sugar prior to removing the solvent is in the range of 20-40%. Dalton et al. discloses the sugar concentration is between 20-50% w/v, and most

preferable about 40% prior to drying [0042]. It would have been obvious to one of ordinary skill in the art to modify the sugar concentration in order to attain the desired viscosity of reservoir forming medium. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or working ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

With respect to claim 27, the modified Volkin et al. discloses the solvent is demetalated prior to the process (pg. 11, line 31 – pg. 12, line 7; pg. 26, lines 22-31; pg. 58, lines 16-20).

Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dev et al. in view of Volkin et al.

With respect to claims 4 and 5, Dev et al. addresses all the limitations of claims 1-3, however fails to expressly disclose the inclusion of a free radical scavenger in combination with the metal ion chelator. Volkin et al. discloses DNA formulations wherein the stabilizing agent that inhibit the degradative effects of free radicals is phosphate buffered ethanol solution in combination with methionine or EDTA (pg. 72, lines 14-24) and Tris buffered EDTA in combination with methionine or ethanol or a combination of methionine and ethanol (pg. 25, lines 12-19). Volkin et al. further discloses the solvent is demetalated prior to the process (pg. 11, line 31 – pg. 12, line 7). It would have been obvious to one of ordinary skill in the art to utilize the DNA formulation of Volkin et al. in order to enhance the stability of the formulation.

Claims 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dev et al. in view of Roser et al. (US 6,290,991).

With respect to claims 6-11, Dev et al. addresses all the limitations of claim 1 and further discloses the solid reservoir medium can be formed of any biocompatible suitably absorbent material or material to which injection substance will adhere (col. 15, lines 42-49). However, Dev et al. fails to expressly disclose the material being a stabilizing polyol. Roser et al. discloses a microneedle having a solid reservoir medium comprising a stabilizing glass-forming polyol, which is preferably trehalose (col. 3, line 67 – col. 4, line 1; col. 7, line 37). It would have been obvious to one of ordinary skill in the art to modify the material used in order to attain a material with the desired release rate. Further, it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice. In re Leshin, 125 USPQ 416.

Claims 1-18, 21 and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roser et al. in view of Volkin et al.

With respect to claims 1-5, 18, 21, 24-26, Roser et al. discloses a DNA pharmaceutical agent delivery device, and the process of making the delivery device, having at least one skin-piercing microneedle which comprises a support member (needle) coated with a solid reservoir medium (stabilizing polyol) containing the DNA pharmaceutical agent (DNA vaccine) (col. 6, lines 5-32; col. 12, lines 25-31, 44-47). Roser et al. fails to expressly disclose the inclusion of a stabilizing agent. Volkin et al.

discloses a DNA vaccine formulation comprising various stabilizing agents that inhibits the degradative effects of free radicals. Volkin et al. discloses the stabilizing agent is one or both of a metal ion chelator (EDTA, TRIS, succinic and malic acid) (pg. 10, lines 14-15; pg. 26, line 32 – pg. 27, line 15) and free radical scavengers (ethanol, methionine) (page 11, lines 4-9; claim 25). Volkin et al. further discloses DNA formulations wherein the stabilizing agent that inhibit the degradative effects of free radicals is phosphate buffered ethanol solution in combination with methionine or EDTA (pg. 72, lines 14-24) and Tris buffered EDTA in combination with methionine or ethanol or a combination of methionine and ethanol (pg. 25, lines 12-19). It would have been obvious to one of ordinary skill in the art to include the stabilizing agent(s) of Volkin et al. in order to provide a stable DNA vaccine.

With respect to claims 6-11, the modified Roser et al. discloses a microneedle having a solid reservoir medium comprising a stabilizing glass-forming polyol, which is preferably trehalose (col. 3, line 67 – col. 4, line 1; col. 7, line 37).

With respect to claims 12-14, the modified Roser et al. discloses the DNA pharmaceutical agent is plasmid DNA (col. 6, line 8), however fails to expressly disclose it being supercoiled plasmid DNA. Volkin et al. discloses the DNA pharmaceutical agent is supercoiled plasmid DNA (pg. 34, lines 8-9), and that after storage at 37°C for 4 weeks, greater than 50% of the DNA remains in its supercoiled form, wherein the DNA is stabilized such that when released the ratio of monomer:dimer supercoiled form is within the range of 0.8-1.2 as evidenced by the method of detection used to detect supercoiled plasmid DNA and the stability data disclosed by the referenced invention

(Tables 5, 9, 10, 13; Figs. 14, 20-24, 28; Examples 5, 11-16, 18). It would have been obvious to one of ordinary skill in the art to utilize supercoiled plasmid DNA since the supercoiled form is more stable than the relaxed circle form, as taught by Volkin et al. (pg. 34, lines 8-9).

With respect to claim 15, the modified Roser et al. discloses the solid reservoir medium provides a quick release or flooding dose of the pharmaceutical agent after administration and will dissolve rapidly to provide initial dosing (col. 12, lines 35-39, 47-49), therefore is considered to release the pharmaceutical agent within 24 hours after insertion of the skin-piercing needle into the skin.

With respect to claims 16 and 17, the modified Roser et al. discloses the microneedle is dimensioned to deliver the DNA pharmaceutical agent into the epidermis or dermis (col. 9, lines 31-43).

With respect to claim 26, the modified Roser et al. fails to expressly disclose the concentration of sugar prior to the removal of the solvent is in the range of 20-40% w/v. However, it would have been obvious to one of ordinary skill in the art to modify the range in order to provide the desired release rate of the pharmaceutical agent. Further, it has been held that where the general conditions of a claim are discloses in the prior art, discovering the optimum or working ranges involves only routine skill in the art. In re Aller, 105USPQ 233.

With respect to claim 27, the modified Roser et al. fails to expressly disclose the solvent being demetalated prior to the process. Volkin et al. discloses the solvent is demetalated prior to the process (pg. 11, line 31 – pg. 12, line 7; pg. 26, lines 22-31; pg.

58, lines 16-20). It would have been obvious to one of ordinary skill in the art to demetalate the solvent prior to the process in order to provide DNA stability.

Claims 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roser et al. in view of Volkin et al. and further in view of Van Nest et al. (US 6,299,884).

With respect to claims 22 and 23, the modified Roser et al. addresses all the limitations of claim 1, however fails to expressly disclose the inclusion of a vaccine adjuvant. Van Nest et al. discloses a vaccine prepared by recombinant DNA techniques where the vaccine having an adjuvant formulation that is an oil-in-water emulsion (col. 2, line 65 – col. 3, line 13; col. 13, lines 39-43). It would have been obvious to one of ordinary skill in that art to have an oil-in-water emulsion in order to stimulate immune responses to molecular antigens, as taught by Van Nest et al. (col. 2, line 65 – col. 3, line 13).

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Eriksson (US 5,697,901) discloses utilizing microneedles to deliver DNA pharmaceutical agents into the skin.

King et al. (US 6,603,998) discloses a system for delivery of DNA vaccines into cells.

Telephone/Fax Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suezu Ellis whose telephone number is (571) 272-2868. The examiner can normally be reached on 8:30am-5pm (Monday-Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharon Kennedy can be reached on (571) 272-4948. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SE

/Sharon E. Kennedy/
Primary Examiner, Art Unit 1615